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NEWS 4 JUL 02 CHEMCATS accession numbers revised
NEWS 5 JUL 02 CA/Capplus enhanced with utility model patents from China
NEWS 6 JUL 16 Capplus enhanced with French and German abstracts
NEWS 7 JUL 18 CA/Capplus patent coverage enhanced
NEWS 8 JUL 26 USPATFULL/USPAT2 enhanced with IPC reclassification
NEWS 9 JUL 30 USGENE now available on STN
NEWS 10 AUG 06 CAS REGISTRY enhanced with new experimental property tags
NEWS 11 AUG 06 BEILSTEIN updated with new compounds
NEWS 12 AUG 06 FSTA enhanced with new thesaurus edition
NEWS 13 AUG 13 CA/Capplus enhanced with additional kind codes for granted patents
NEWS 14 AUG 20 CA/Capplus enhanced with CAS indexing in pre-1907 records
NEWS 15 AUG 27 Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS 16 AUG 27 USPATOLD now available on STN
NEWS 17 AUG 28 CAS REGISTRY enhanced with additional experimental spectral property data
NEWS 18 SEP 07 STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS 19 SEP 13 FORIS renamed to SOFIS
NEWS 20 SEP 13 INPADOCDB enhanced with monthly SDI frequency
NEWS 21 SEP 17 CA/Capplus enhanced with printed CA page images from 1967-1998
NEWS 22 SEP 17 Capplus coverage extended to include traditional medicine patents

NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

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FILE LAST UPDATED: 19 Sep 2007 (20070919/ED)

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```
=> (HIV envelope protein)
    74183 HIV
      100 HIVS
    74200 HIV
      (HIV OR HIVS)
    59651 ENVELOPE
    10260 ENVELOPES
    65690 ENVELOPE
      (ENVELOPE OR ENVELOPES)
    2054953 PROTEIN
    1441050 PROTEINS
    2394491 PROTEIN
      (PROTEIN OR PROTEINS)
L1      348 (HIV ENVELOPE PROTEIN)
      (HIV(W) ENVELOPE(W) PROTEIN)

=> CD4 (l) complex
    57847 CD4
    1362886 COMPLEX
    753189 COMPLEXES
    1659926 COMPLEX
      (COMPLEX OR COMPLEXES)
L2      6466 CD4 (L) COMPLEX

=> L1 and L2
L3      29 L1 AND L2

=> antibody and L3
    317123 ANTIBODY
    377349 ANTIBODIES
    501767 ANTIBODY
      (ANTIBODY OR ANTIBODIES)
L4      19 ANTIBODY AND L3

=> (DB-81)
    29602 DB
    1490 DBS
    30962 DB
      (DB OR DBS)
```

159066 81
L5 3 (DB-81)
(DB(W)81)

=> D L5 IBIB ABS 1-3

L5 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:741925 CAPLUS

DOCUMENT NUMBER: 133:296587

TITLE: Preparation of camptothecin analogs for pharmaceutical use in the treatment of cancer

INVENTOR(S): Curran, Dennis P.; Bom, David; Burke, Thomas G.

PATENT ASSIGNEE(S): University of Pittsburgh, USA; University of Kentucky Research Foundation

SOURCE: PCT Int. Appl., 130 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

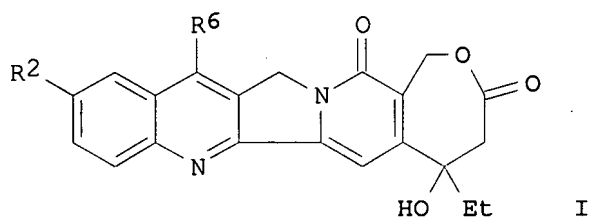
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|-------------|
| WO 2000061146 | A1 | 20001019 | WO 2000-US9401 | 20000407 |
| W: | AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW | | | |
| RW: | GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| US 6207832 | B1 | 20010327 | US 1999-290019 | 19990409 |
| CA 2369270 | A1 | 20001019 | CA 2000-2369270 | 20000407 |
| AU 200042177 | A | 20001114 | AU 2000-42177 | 20000407 |
| AU 781302 | B2 | 20050512 | | |
| EP 1173180 | A1 | 20020123 | EP 2000-921919 | 20000407 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | |
| JP 2002541201 | T | 20021203 | JP 2000-610479 | 20000407 |
| NZ 529569 | A | 20031219 | NZ 2000-529569 | 20000407 |
| NZ 514635 | A | 20040227 | NZ 2000-514635 | 20000407 |
| US 2001003779 | A1 | 20010614 | US 2000-728031 | 20001130 |
| US 6410731 | B2 | 20020625 | | |
| US 2003088101 | A1 | 20030508 | US 2002-164326 | 20020606 |
| US 6809103 | B2 | 20041026 | | |
| HK 1046374 | A1 | 20070824 | HK 2002-107997 | 20021104 |
| US 2005014775 | A1 | 20050120 | US 2004-919068 | 20040816 |
| US 7220860 | B2 | 20070522 | | |
| PRIORITY APPLN. INFO.: | | | US 1999-290019 | A 19990409 |
| | | | WO 2000-US9401 | W 20000407 |
| | | | US 2000-728031 | A3 20001130 |
| | | | US 2002-164326 | A3 20020606 |

OTHER SOURCE(S): MARPAT 133:296587

GI



AB Camptothecin analogs, such as I [R2 = H, OH, NH2, acyl, alkoxy, acyloxy, etc.; R6 = silyl, silylalkyl, silylalkenyl, silylalkynyl, etc.], were prepared for use as antitumor agents. Thus, (+)-10-amino-7-(tert-butylidimethylsilyl)homocamptothecin, a.k.a. DB 90, was prepared via a multistep synthetic sequence starting from 4-ethyl-8-methoxy-6-(trimethylsilyl)-1H-pyrano[3,4-c]pyridine, tert-Bu bromoacetate, 1-bromo-3-tert-butylidimethylsilyl-2-propyne, and 4-(tert-Butyloxycarbonylamino)phenylisocyanate. The prepared homocamptothecins were tested for activity against MDA-MB-435 tumorigenic metastatic human breast cancer cells.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:455126 CAPLUS

DOCUMENT NUMBER: 131:299588

TITLE: Novel A,B,E-Ring-Modified Camptothecins Displaying High Lipophilicity and Markedly Improved Human Blood Stabilities

AUTHOR(S): Bom, David; Curran, Dennis P.; Chavan, Ashok J.; Kruszewski, Stefan; Zimmer, Stephen G.; Fraley, Kimberly A.; Burke, Thomas G.

CORPORATE SOURCE: Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA

SOURCE: Journal of Medicinal Chemistry (1999), 42(16), 3018-3022

CODEN: JMCMAR; ISSN: 0022-2623

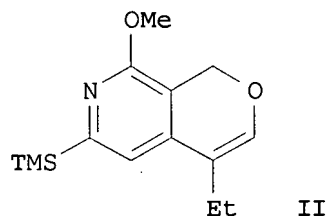
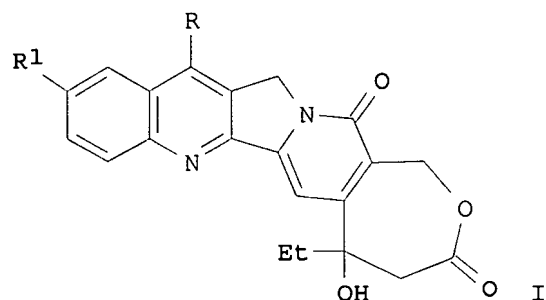
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 131:299588

GI



AB The camptothecins I (R = Me3CSiMe2, Me3Si; R1 = NH2, OH, H) were prepared starting from enol ether II. A variety of anal. and biophys. methods were employed to compare the blood component interactions and blood stabilities of I with camptothecin. I are potent topoisomerase I inhibitors that are stable not only in the mouse blood but human blood.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1983:535033 CAPLUS

DOCUMENT NUMBER: 99:135033

TITLE: Elimination- and biodistribution studies of [14C]dodecylbenzenesulfonate in rats, following low dosing in the daily diet and a single i.p. administration

AUTHOR(S): Lay, Jan P.; Klein, Werner; Korte, Friedhelm

CORPORATE SOURCE: Inst. Oekol. Chem., Ges. Strahlen Umweltforsch. m.b.H. Muenchen, Neuherberg, D-8042, Fed. Rep. Ger.

SOURCE: Toxicology Letters (1983), 17(1-2), 187-92

CODEN: TOLED5; ISSN: 0378-4274

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 14C-labeled dodecylbenzenesulfonate (DBS) [1886-81-3] was administered daily in the diet at a concentration of 1.4 mg/kg to rats for 5 wk. From the total uptake (1.213 mg/animal) of DBS, 81.8% was excreted during the dosing period; 52.4% in the feces and 29.4% in the urine. Low levels of [14C]DBS-derived residues were detected in all tissues analyzed on day 35 of the experiment. Following 1 wk on normal diet only 7.8% of the nominally stored amount of 14C was found in the excreta. Single i.p. application of 0.385 mg [14C]DBS/rat (2.26 mg/kg) resulted in a total elimination of 94.5% within 10 days; 84.7% of the dose was eliminated in the 1st 24 h. All fecal and renal [14C]DBS-derived activity consisted of highly polar metabolites.

=> D L4 IBIB ABS 1-19

L4 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:284235 CAPLUS

DOCUMENT NUMBER: 146:315026

TITLE: HIV gp120 crystal structure and its use to identify immunogens

INVENTOR(S): Kwong, Peter D.; Zhoh, Tongqing; Xu, Ling; Nabel, Gary; Dey, Barna; Wyatt, Richard

PATENT ASSIGNEE(S): The United States Dept. Of Health & Human Services, USA

SOURCE: PCT Int. Appl., 187pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2007030637 | A2 | 20070315 | WO 2006-US34882 | 20060906 |
| WO 2007030637 | A9 | 20070518 | | |
| WO 2007030637 | A3 | 20070621 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW | | | |
| RW: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, | | | |

KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA
PRIORITY APPLN. INFO.: US 2005-713725P P 20050906
US 2005-729878P P 20051024
US 2005-731627P P 20051028
US 2006-832458P P 20060720

AB The authors disclose the engineering of the envelope protein of HIV to provide a stabilized conformation reflective of the CD4-bound state. In one example, a crystal structure is provided for a disulfide-stabilized gp120 envelope protein in complex with the CD4-binding site antibody b12.

L4 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:227988 CAPLUS

DOCUMENT NUMBER: 146:272539

TITLE: Use of HIV envelope/CD4 complexes
for the generation antibodies and as
immunogenic complexes

INVENTOR(S): Wang, Jinhai; Norcross, Michael

PATENT ASSIGNEE(S): Government of the United States of America, as
Represented by the Secretary, USA

SOURCE: PCT Int. Appl., 45pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2007025276 | A2 | 20070301 | WO 2006-US33635 | 20060825 |
| WO 2007025276 | A3 | 20070531 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW | | | |
| RW: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA | | | |

PRIORITY APPLN. INFO.: US 2005-711985P P 20050825

AB The authors disclose antibodies, vaccines, and immunogenic compns., for the treatment and prevention of HIV infection. In one example, , the authors elicit HIV neutralizing antibodies by immunization with gp120 complexed with NIH3T3 cells transgenic for human CD4.

L4 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:1160381 CAPLUS

DOCUMENT NUMBER: 143:384738

TITLE: A single-cycle vaccine vector based on vesicular stomatitis virus can induce immune responses comparable to those generated by a replication-competent vector

AUTHOR(S): Publicover, Jean; Ramsburg, Elizabeth; Rose, John K.

CORPORATE SOURCE: Section of Microbial Pathogenesis, Yale University
School of Medicine, New Haven, CT, 06510, USA

SOURCE: Journal of Virology (2005), 79(21), 13231-13238

CODEN: JOVIAM; ISSN: 0022-538X

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Live attenuated vaccine vectors based on recombinant vesicular stomatitis virus (VSV) are effective in several viral disease models. In this study, the authors asked if a VSV vector capable of only a single cycle of replication might be an effective alternative to replication-competent VSV vectors. The authors compared the cellular immune responses to human immunodeficiency virus (HIV) envelope protein (Env) expressed by replication-competent and single-cycle VSV vectors and also examined the antibody response to Env. The single-cycle vector was grown by complementation with VSV G protein and then tested initially for immunogenicity when given by four different routes. When given by the i.m. route in mice, the authors found that the single-cycle vector was equivalent to the replication-competent VSV vector in generating high-level primary and memory CD8 T-cell responses as well as antibody responses to Env. Cellular responses were analyzed using major histocompatibility complex class I tetramers and direct measurement of cytotoxic T-lymphocyte activity in vivo. The authors also found that the recall responses after boosting were equivalent in animals vaccinated with replication-competent or single-cycle vectors. Addnl., the authors observed recall and heightened memory responses after boosting animals with a single-cycle vector complemented with G protein from a different vesiculovirus. Because expression of HIV Env by G-deleted VSV might allow replication in human cells expressing CD4, the authors generated a single-cycle VSV recombinant expressing a secreted form of the HIV Env protein. This virus was just as effective as the recombinant expressing the membrane-anchored Env protein at producing CD8 T cells and antibody responses.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:706206 CAPLUS

DOCUMENT NUMBER: 141:275960

TITLE: Identification and characterization of a new cross-reactive human immunodeficiency virus type 1-neutralizing human monoclonal antibody

AUTHOR(S): Zhang, Mei-Yun; Xiao, Xiaodong; Sidorov, Igor A.; Choudhry, Vidita; Cham, Fatim; Zhang, Peng Fei; Bouma, Peter; Zwick, Michael; Choudhary, Anil; Montefiori, David C.; Broder, Christopher C.; Burton, Dennis R.; Quinnan, Gerald V., Jr.; Dimitrov, Dimitar S.

CORPORATE SOURCE: Human Immunovirology Group, Laboratory of Experimental and Computational Biology, Center for Cancer Research, National Cancer Institute-Frederick, Frederick, MD, USA

SOURCE: Journal of Virology (2004), 78(17), 9233-9242
CODEN: JOVIAM; ISSN: 0022-538X

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The identification and characterization of new human monoclonal antibodies (hMAbs) able to neutralize primary human immunodeficiency virus type 1 (HIV-1) isolates from different subtypes may help in understanding the mechanisms of virus entry and neutralization and in the development of entry inhibitors and vaccines. For enhanced selection of broadly cross-reactive antibodies, soluble HIV-1 envelope glycoproteins (Envs proteins) from two isolates complexed with two-domain soluble CD4 (sCD4) were alternated during panning of a phage-displayed human antibody library; these two Env proteins (89.6 and IIIB gp140s), and one addnl. Env (JR-FL gp120) alone and complexed with sCD4 were used for screening. An antibody with relatively long HCDR3 (17 residues), designated m14, was identified that bound to all antigens and neutralized heterologous HIV-1 isolates in multiple assay formats. Fab m14 potentially neutralized selected

well-characterized subtype B isolates, including JRCSF, 89.6, IIIB, and Yu2. IgG1 m14 was more potent than Fab m14 and neutralized 7 of 10 other clade B isolates; notably, although the potency was on average significantly lower than that of IgG1 b12, IgG1 m14 neutralized two of the isolates with significantly lower 50% inhibitory concns. than did IgG1 b12. IgG1 m14 neutralized four of four selected clade C isolates with potency higher than that of IgG1 b12. It also neutralized 7 of 17 clade C isolates from southern Africa that were difficult to neutralize with other hMAbs and sCD4. IgG1 m14 neutralized four of seven primary HIV-1 isolates from other clades (A, D, E, and F) much more efficiently than did IgG1 b12; for the other three isolates, IgG b12 was much more potent. Fab m14 bound with high (nanomolar range) affinity to gp120 and gp140 from various isolates; its binding was reduced by soluble CD4 and antibodies recognizing the CD4 binding site (CD4bs) on gp120, and its footprint as defined by alanine-scanning mutagenesis overlaps that of b12. These results suggest that m14 is a novel CD4bs cross-reactive HIV-1-neutralizing antibody that exhibits a different inhibitory profile compared to the only known potent broadly neutralizing CD4bs human antibody, b12, and may have implications for understanding the mechanisms of immune evasion and for the development of inhibitors and vaccines.

REFERENCE COUNT: 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:142990 CAPLUS

DOCUMENT NUMBER: 140:180126

TITLE: Vaccine compositions comprising HIV envelope protein and CD4 for generating monoclonal anti-HIV antibodies and for immunotherapies

INVENTOR(S): Lusso, Paolo; Burastero, Samuele E.

PATENT ASSIGNEE(S): Fondazione Centro San Raffaele Del Monte Tabor, Italy

SOURCE: PCT Int. Appl., 74 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2004014420 | A1 | 20040219 | WO 2003-IB3665 | 20030812 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2497662 | A1 | 20040219 | CA 2003-2497662 | 20030812 |
| AU 2003253187 | A1 | 20040225 | AU 2003-253187 | 20030812 |
| EP 1545602 | A1 | 20050629 | EP 2003-784418 | 20030812 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| US 2006142219 | A1 | 20060629 | US 2005-524549 | 20050913 |
| PRIORITY APPLN. INFO.: | | | GB 2002-18817 | A 20020813 |
| | | | WO 2003-IB3665 | W 20030812 |

AB (A) Pharmaceutical composition for treating/preventing HIV comprising (i) a polynucleotide encoding HIV envelope protein and (ii) a polynucleotide encoding CD4 receptor protein or; (i)

a polynucleotide encoding HIV envelope protein and (iii) a CD4 receptor protein or; a fixed cell expressing an HIV envelope protein complexed with a CD4 receptor protein also disclosed are (B) pharmaceutical compns. for treating/preventing HIV comprising an antibody immunospecific for a fixed cell expressing an HIV envelope protein complexes with a CD4 receptor protein. The binding of the CD4 to the HIV envelope protein, i.e. gp120 (or gp160), exposes hidden epitopes that may be used as targets in immunotherapies; the presentation of the gp120 and CD4 in the present forms is said to overcome problems with prior art soluble gp120-CD4 complexes. Also disclosed are genetic vectors encoding and expression HIV-1 gp120 and CD4 or their fusion protein for treating T or CD4+ T cell-mediated immune diseases and inflammation.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:80848 CAPLUS
DOCUMENT NUMBER: 140:144692
TITLE: IgG Fc/HIV-gp120/C3d fusion protein
INVENTOR(S): Haynes, Barton F.; Montefiori, David C.
PATENT ASSIGNEE(S): Duke University, USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2004009785 | A2 | 20040129 | WO 2003-US22917 | 20030723 |
| WO 2004009785 | A3 | 20040805 | | |
| W: | | | | |
| AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: | | | | |
| GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2493706 | A1 | 20040129 | CA 2003-2493706 | 20030723 |
| AU 2003256671 | A1 | 20040209 | AU 2003-256671 | 20030723 |
| BR 2003012808 | A | 20050419 | BR 2003-12808 | 20030723 |
| EP 1523492 | A2 | 20050420 | EP 2003-765923 | 20030723 |
| R: | | | | |
| AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| CN 1668633 | A | 20050914 | CN 2003-817196 | 20030723 |
| JP 2006509496 | T | 20060323 | JP 2004-523297 | 20030723 |
| ZA 2004010324 | A | 20060726 | ZA 2004-10324 | 20041222 |
| MX 2005PA00874 | A | 20050323 | MX 2005-PA874 | 20050121 |
| US 2006014148 | A1 | 20060119 | US 2005-518523 | 20050817 |

PRIORITY APPLN. INFO.: US 2002-397605P P 20020723
WO 2003-US22917 W 20030723

AB The present invention relates, in general, to an immunogen and, in particular, to an immunogen for inducing antibodies that neutralize a wide spectrum of HIV primary isolates. The invention also relates to a method of inducing anti-HIV antibodies using same. In one example, the immunogen comprises a fusion protein of complement C3d, HIV envelope protein, and IgG Fc

fragment.

L4 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:814665 CAPLUS
DOCUMENT NUMBER: 137:336719
TITLE: Chimeric protein comprising virus coat protein and
virus receptor for producing antibody and
for preventing viral infection
INVENTOR(S): Devico, Anthony Louis; Fouts, Timothy R.; Tuskan,
Robert G.
PATENT ASSIGNEE(S): University of Maryland Biotechnology Institute, USA
SOURCE: U.S. Pat. Appl. Publ., 71 pp., Cont.-in-part of U.S.
Ser. No. 684,026.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----------------|--|----------|-----------------|----------|
| US 2002155121 | A1 | 20021024 | US 2001-934060 | 20010821 |
| US 6908612 | B2 | 20050621 | | |
| CA 2457414 | A1 | 20030227 | CA 2002-2457414 | 20020821 |
| WO 2003016333 | A2 | 20030227 | WO 2002-US26543 | 20020821 |
| WO 2003016333 | A3 | 20030731 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| AU 2002355966 | A1 | 20030303 | AU 2002-355966 | 20020821 |
| AU 2002355966 | B2 | 20070118 | | |
| EP 1425036 | A2 | 20040609 | EP 2002-794930 | 20020821 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | |
| BR 2002012093 | A | 20041130 | BR 2002-12093 | 20020821 |
| CN 1561229 | A | 20050105 | CN 2002-819350 | 20020821 |
| JP 2005503147 | T | 20050203 | JP 2003-521255 | 20020821 |
| MX 2004PA01585 | A | 20050307 | MX 2004-PA1585 | 20040220 |
| ZA 2004002190 | A | 20050506 | ZA 2004-2190 | 20040318 |
| US 2005221445 | A1 | 20051006 | US 2005-124027 | 20050506 |

PRIORITY APPLN. INFO.:
US 1999-158321P P 19991008
US 2000-684026 A2 20001006
US 2001-934060 A 20010821
WO 2002-US26543 W 20020821

AB The invention relates to chimeric mols. comprising a virus coat sequence and a receptor sequence that can interact with each other to form a complex that is capable of binding a co-receptor. Such chimeric mols. therefore exhibit functional properties characteristic of a receptor-coat protein complex and are useful as agents that inhibit virus infection of cells due to occupancy of a co-receptor present on the cell. In particular aspects, the chimeric polypeptide includes an immunodeficiency virus envelope polypeptide, such as that of HIV, SIV, FIV, FeLV, FPV and herpes virus. The coat protein is e.g. HIV envelope protein or gp120, and the receptor is e.g. CD4 D1D2 domains and CD4M9 sequence.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:229525 CAPLUS
DOCUMENT NUMBER: 136:382380
TITLE: Identification of components of protein complexes
using a fluorescent photo-cross-linker and mass
spectrometry
AUTHOR(S): Wine, Robert N.; Dial, John M.; Tomer, Kenneth B.;
Borchers, Christoph H.
CORPORATE SOURCE: Laboratory of Toxicology and Laboratory of Structural
Biology, National Institute of Environmental Health
Sciences/NIH, Research Triangle Park, NC, 27713, USA
SOURCE: Analytical Chemistry (2002), 74(9), 1939-1945
CODEN: ANCHAM; ISSN: 0003-2700
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This study describes a novel method for improving the specific
recognition, detection, and identification of proteins involved in
multiprotein complexes. The method is based on a combination of
coimmunopptn., chemical crosslinking, and specific fluorescent tagging of
protein components in close association with one another. Specific
fluorescent tagging of the protein complex components was
achieved using the cleavable, fluorescent cross-linker sulfo succinimidyl
2-(7-azido-4-methylcoumarin-3-acetamido) ethyl-1,3'-dithiopropionate
(SAED). Following dissociation and separation by SDS-PAGE, the fluorescently
tagged proteins are then visualized by UV illumination, excised, and,
following in-gel digestion, identified by mass spectrometry. In this
study, a complex of the HIV-envelope
protein gp120 and its cellular receptor CD4 was used as
a model system. The sensitivity of detection of fluorescent SAED-labeled
proteins in SDS gels, and the sensitivity of the mass spectrometric
identification of fluorescent proteins after in-gel digestion, is in the
range of a few hundred femtomoles of protein. This sensitivity is
comparable to that achieved with silver-staining techniques, but
fluorescence detection is protein independent and no background
interference occurs. Furthermore, fluorescence labeling is significantly
more compatible with mass spectrometric identification of proteins than is
silver staining. The first application of this strategy was in the
investigation of the mechanism of spermiation, the process by which mature
spermatids sep. from Sertoli cells. For the coimmunopptn. experiment, an
antibody against paxillin, a protein involved in spermatid-Sertoli
cell junctional complexes, was used. More components of the
paxillin protein complex were visible by fluorescence detection
of SAED-labeled proteins than were visible on comparable silver-stained
gels. Mass spectrometric anal. of the fluorescently labeled proteins
identified integrin $\alpha 6$ precursor as a protein associated in a
complex with paxillin. The identification of integrin $\alpha 6$
precursor was confirmed by Western blot anal. and verifies the
applicability of this novel approach for identifying proteins involved in
protein complexes.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:921226 CAPLUS
DOCUMENT NUMBER: 137:88058
TITLE: Dexamethasone inhibits CD4 T cell deletion mediated by
macrophages from human immunodeficiency virus-infected
persons
AUTHOR(S): Orlikowsky, Thorsten W.; Wang, Z. Q.; Dudhane, Anita;
Dannecker, Gunther E.; Niethammer, Dietrich; Wormser,
Gary P.; Hoffmann, Michael K.; Horowitz, Harold W.
CORPORATE SOURCE: Departments of Microbiology and Immunology, Division

of Infectious Diseases, New York Medical College,
Valhalla, NY, USA

SOURCE: Journal of Infectious Diseases (2001), 184(10),
1328-1330
CODEN: JIDIAQ; ISSN: 0022-1899

PUBLISHER: University of Chicago Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Prednisolone slows the loss of CD4 T cells in individuals with human immunodeficiency virus (HIV) disease and inhibits antigen-induced apoptosis of recently HIV-infected CD4 cells in vitro. This study investigated whether dexamethasone inhibits the ability of macrophages to delete CD4 T cells via anti-CD4 antibody or immune-complexed HIV envelope protein gp120. Peripheral blood mononuclear cells from HIV-neg. persons were incubated with CD4-reactive ch412 monoclonal antibody or with gp120/IgG immune complexes and resident macrophages, with and without dexamethasone. Dexamethasone inhibited CD4 cell deletion in a dose-dependent manner. The deletion of normal CD4 cells by macrophages from HIV-infected patients also was inhibited by dexamethasone. Furthermore, up-regulation of CD95 expression on T cells exposed to anti-CD4 and gp120/IgG, which predisposes T cells to CD95-mediated apoptosis, is inhibited by dexamethasone in a dose-dependent fashion. Dexamethasone inhibits the macrophage-mediated deletion of CD4 lymphocytes in HIV-infected persons.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:400785 CAPLUS

DOCUMENT NUMBER: 131:213014

TITLE: The implication of the chemokine receptor CXCR4 in HIV-1 envelope protein-induced apoptosis is independent of the G protein-mediated signaling

AUTHOR(S): Blanco, Julia; Jacotot, Etienne; Cabrera, Cecilia; Cardona, Ana; Clotet, Bonaventura; De Clercq, Erik; Este, Jose A.

CORPORATE SOURCE: Institut de Recerca de la SIDA-Caixa, Laboratori de Retrovirologia, Hospital Universitari Germans Trias i Pujol, Catalonia, Spain

SOURCE: AIDS (London) (1999), 13(8), 909-917
CODEN: AIDSET; ISSN: 0269-9370

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Objective: The envelope glycoprotein complex (gp120/gp41)n of HIV-1 is one of the viral products responsible for increased apoptosis in HIV infection. Here the role of the chemokine receptor CXCR4 in HIV-1 envelope protein-induced apoptosis was investigated. Methods: Apoptosis occurring in cocultures of chronically HIV-1 IIIB-infected cells with CD4 target cells expressing the CXCR4 receptor was quantified by terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) or propidium iodide staining followed by fluorescent antibody cell sorting, which allows the evaluation of single-cell killing. Moreover global (single cell- and syncytium-associated) apoptosis was quantified by a new radioactive TUNEL-derived assay. Results: By using these different techniques it was shown that single and syncytium-forming CD4 T cells die by apoptosis upon contact with envelope protein expressing cells independently of viral replication. Moreover, both the CXCR4 agonist SDF-1 α , and the antagonist AMD3100, showed inhibitory effects on HIV-1 envelope protein-induced apoptosis in the CD4 T-cell subset of peripheral blood mononuclear cells and CD4 cell lines. CXCR4 signaling-induced by HIV-1 envelope proteins in CD4 T

cells was not detected. Furthermore, it was shown that envelope protein-induced apoptosis can occur after treating target cells with the Gi-protein inhibitor pertussis toxin. Conclusions: Evidence is provided for a role of CXCR4 in the mechanisms of HIV envelope protein-induced pathogenesis, contributing to selective CD4 cell killing. The results suggest that CXCR4 is involved in HIV-1-induced apoptosis; however, this role does not appear to involve G-protein-mediated CXCR4 signaling.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:305752 CAPLUS

DOCUMENT NUMBER: 129:107912

TITLE: TCD4+ lymphocytes apoptosis induced by HIV envelope: implication of the B7 cosignal

AUTHOR(S): Da Mota, C. Coito; Bomsel, M.

CORPORATE SOURCE: INSERM U. 332 ICGM, Paris, 75014, Fr.

SOURCE: HIV and Cytokines (1997), 251-259. Editor(s): Guenounou, Moncef. Editions INSERM: Paris, Fr. CODEN: 66AJA9

DOCUMENT TYPE: Conference

LANGUAGE: English

AB In this report, the authors examined early mechanisms mediated by HIV envelope protein on CD4+ T-cells leading to their apoptosis. Apoptosis was measured following priming of CD4+ cells with envelope-transfected HeLa cells and subsequent activation by pokeweed mitogen or with anti-CD3 antibodies.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:250209 CAPLUS

DOCUMENT NUMBER: 124:306650

TITLE: Inhibition of HIV-1 in cell culture by synthetic humate analogs derived from hydroquinone: mechanism of inhibition

AUTHOR(S): Schneider, Josef; Weis, Roland; Maenner, Christine; Kary, Beate; Werner, Albrecht; Sfubert, Bernhard J.; Riede, Urs N.

CORPORATE SOURCE: Abteilung Virol., Univ. Freiburg, Freiburg, D-79104, Germany

SOURCE: Virology (1996), 218(2), 389-95
CODEN: VIRLAX; ISSN: 0042-6822

PUBLISHER: Academic

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Humic acids are natural constituents of soil and ground water and mainly consist of mixts. of polycyclic phenolic compds. A similar complex of compds. with a mean size of about 1000 Da, designated HS-1500, was synthesized by oxidation of hydroquinone. HS-1500 inhibited HIV-1 infection of MT-2 cells with an IC50 of 50-300 ng/mL and showed a mean cell toxicity of about 600 µg/mL. Inhibition of HIV-induced syncytium formation was observed at 10-50 µg/mL. Treatment of free and cell-attached HIV with HS-1500 irreversibly reduced its infectivity, whereas the susceptibility of target cells for the virus was not impaired by treatment prior to infection. The HIV envelope protein gp120SU bound to sepharose-coupled HS-1500 and could be eluted by high salt and detergent. HS-1500 interfered with the CD4-induced proteolytic cleavage of the V3 loop of virion gp120SU. Furthermore, binding of V3 loop-specific antibodies was irreversibly inhibited, whereas binding of soluble CD4 to gp120SU on virus and infected cells was not affected. In conclusion, our data suggest, that the synthetic humic acid analog inhibits the infectivity of

HIV particles by interference with a V3 loop-mediated step of virus entry.

L4 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:46180 CAPLUS

DOCUMENT NUMBER: 124:84311

TITLE: Humoral response to oligomeric human immunodeficiency virus type 1 envelope protein

AUTHOR(S): Richardson, Thomas M., Jr.; Stryjewski, Brenda L.; Broder, Christopher C.; Hoxie, James A.; Mascola, John R.; Earl, Patricia L.; Doms, Robert W.

CORPORATE SOURCE: Dep. Pathology, Univ. Pennsylvania, Philadelphia, PA, 19104, USA

SOURCE: Journal of Virology (1996), 70(2), 753-62

CODEN: JOVIAM; ISSN: 0022-538X

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The humoral immune response to human immunodeficiency virus type 1 (HIV-1) is often studied by using monomeric or denatured envelope proteins (Env). However, native HIV-1 Env complexes that maintain quaternary structure elicit immune responses that are qualitatively distinct from those seen with monomeric or denatured Env. To more accurately assess the levels and types of antibodies elicited by HIV-1 infection, the authors developed an antigen capture ELISA using a soluble, oligomeric form of HIV-1IIIB Env (gp140) that contains gp120 and the gp41 ectodomain. The gp140, captured by various monoclonal antibodies (MAbs), retained its native oligomeric structure: it bound CD4 and was recognized by MAbs to conformational epitopes in gp120 and gp41, including oligomer-specific epitopes in gp41. The authors compared the reactivities of clade B and clade E serum samples to captured Env preparations and found that while both reacted equally well with oligomeric gp140, clade B sera reacted more strongly with monomeric gp120 than did clade E samples. However, these differences were minimized when gp120 was captured by a V3 loop MAb, which may lead to increased exposure of the CD4 binding site. The authors also measured the ability of serum samples to block binding of MAbs to epitopes in gp120 and gp41. Clade B serum samples consistently blocked binding of oligomer-dependent MAbs to gp41 and, to a slightly lesser extent, MAbs to the CD4 binding site in gp120. Clade F serum samples showed equivalent or greater blocking of oligomer-dependent gp41 antibodies and considerably less blocking of CD4-binding-site MAbs. Finally, the authors found that <5% of the antibodies in clade B sera bound to epitopes present only in monomeric gp120, 30% bound to epitopes present in both monomeric gp120 and oligomeric gp140, and 70% bound to epitopes present in oligomeric gp140, which includes gp41. Thus, captured oligomeric Env closely reflects the antigenic characteristics of Env protein on the surface of virions and infected cells, retains highly conserved epitopes that are recognized by antibodies raised against different clades, and makes it possible to detect a much greater fraction of total anti-HIV-1 Env activity in sera than does native monomeric gp120.

L4 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:937812 CAPLUS

DOCUMENT NUMBER: 123:337279

TITLE: Human immunodeficiency virus type 1 envelope protein does not stimulate either prostaglandin formation or the expression of prostaglandin H synthase in THP-1 human monocytes/macrophages

AUTHOR(S): Hui, Rutai; Curtis, John F.; Sumner, Martina T.; Shears, Stephen B.; Glasgow, Wayne C.; Eling, Thomas E.

CORPORATE SOURCE: Lab. Cell. Mol. Pharmacol., Natl. Inst. Environ. Health Sci., Research Triangle Park, NC, 27709, USA

SOURCE: Journal of Virology (1995), 69(12), 8020-6

CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Prostaglandin E2 is observed at elevated levels during human immunodeficiency virus (HIV) infection and thus may contribute to the HIV-dependent immunosuppression. The mechanisms responsible for this increase are not understood. Evidence indicates that the viral envelope proteins perturb membrane signaling mediated by the CD4 receptor, suggesting that the free envelope protein and/or the intact virus may be responsible for the increase in prostaglandin E2 levels. In this study, we have used THP-1 human monocytes and THP-1 cells differentiated by 12-O-tetradecanoylphorbol-13-acetate treatment into macrophages to determine if the HIV envelope protein, gp120, or an anti-CD4 receptor antibody stimulates prostaglandin formation by interacting with the CD4 receptor. Incubation of THP-1 cells with OKT4A antibody greatly stimulated the CD4-p56lck receptor complex as estimated by enhanced p56lck autophosphorylation, while the gp120 gave small but significant responses. Monocytic THP-1 cells poorly metabolized arachidonic acid to prostaglandin E2 and thromboxane B2 as measured by high-pressure liquid chromatog. anal. Western blot (immunoblot) and Northern (RNA) blot analyses revealed that unstimulated monocytes expressed little prostaglandin H synthase 1 and 2 (PGHS-1 and -2). Incubation of the monocytes with lipopolysaccharide, OKT4A, or gp120 did not increase the formation of prostaglandins. The expression of PGHS-1 or PGHS-2 was also not increased. Differentiation of the monocytes to macrophages by 12-O-tetradecanoylphorbol-12-acetate treatment resulted in increased expression of PGHS-1 and increased formation of prostaglandins compared with that for the monocytes. Lipopolysaccharide stimulation of the macrophages increased the formation of prostaglandins and increased the expression of PGHS-2 in the macrophages. However, OKT4A or gp120 preparation, at concns. that stimulated p56lck autophosphorylation, did not enhance the formation of prostaglandins or the expression of PGHS-1 or PGHS-2. OKT4A and gp120 also did not stimulate the release of arachidonic acid, indicating that phospholipase A2 was not activated by the CD4 receptor in either the THP-1 monocytes or macrophages. These results indicate that activation of the CD4-p56lck receptor signal transduction pathway by the HIV envelope protein does not increase prostaglandin formation.

L4 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:814168 CAPLUS
DOCUMENT NUMBER: 123:329310
TITLE: Use of CD4/GP120 interactions in the development of anti-HIV drugs and vaccines
AUTHOR(S): Gershoni, J.
CORPORATE SOURCE: Dept. Cell Research and Immunology, Tel-Aviv Univ., Israel
SOURCE: Report (1994), Order No. AD-A282385, 30 pp. Avail.: NTIS
From: Gov. Rep. Announce. Index (U. S.) 1994, 94(22), Abstr. No. 463,676
DOCUMENT TYPE: Report
LANGUAGE: English

AB The HIV envelope protein, gp120 binds to the CD4 cell surface protein and thereby the virus enters T4 helper lymphocytes. This process of virus entry might be associated with presentation of unique epitopes of the gp120 that become revealed only as a result of virus binding to its target cell. The purpose of this research has been to identify cryptic epitopes that become accessible due to induced conformational changes that result from that complex formation of gp120 with CD4. Thus CD4/gp120 complexes have been used to immunize mice and monoclonal

antibodies have been generated. At least 7 antibodies have been identified as having preferred affinity for the above complex. These antibodies are now being characterized. They represent 3 distinct epitopes as has been determined by competitive ELISA assays. Moreover, using a syncytium assay they have been evaluated for their neutralizing activity.

L4 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:204298 CAPLUS

DOCUMENT NUMBER: 122:29538

TITLE: The mixotope: a combinatorial peptide library as a T cell and B cell immunogen

AUTHOR(S): Estaquier, Jerome; Gras-Masse, Helene; Boutillon, Christophe; Ameisen, Jean-Claude; Capron, Andre; Tartar, Andre; Auriault, Claude

CORPORATE SOURCE: Cent. Immunol. maladies transmissibles allergiques, INSERM, Fr.

SOURCE: European Journal of Immunology (1994), 24(11), 2789-95
CODEN: EJIMAF; ISSN: 0014-2980

PUBLISHER: VCH

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors report a new approach in peptide vaccine strategy based on combinatorial synthesis. A library of 7.5 + 105 related peptides, termed mixotope, was derived from the sequence of the third hypervariable domain (V3 loop) of the human immunodeficiency virus (HIV) envelope protein. This preparation induced a strong immune response in all syngeneic and outbred rodents tested. The response directed against the mixotope included antibodies, CD4 + T helper cells (TH1 and TH2) and CD8+ T cells. In rodents immunized with the mixotope, the T cell response directed against individual V3 peptide sequences (BRU, MN, RF, SF2, and ELI) as measured by T cell proliferation and interleukin (IL)-2 production, was found to be major histocompatibility complex haplotype-dependent. However, addnl. expts. performed in mice indicated that selectivity was less restrictive when using IL-3 secretion to explore T cell activation. This combinatorial antigen could be considered as a series of agretopic motifs framing a multiplicity of closely related epitopes for T cell recognition and able to elicit a T cell and B cell repertoire. This new construct may therefore provide a basis for the design of future vaccine strategies.

L4 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1994:555453 CAPLUS

DOCUMENT NUMBER: 121:155453

TITLE: Deletion of T lymphocytes in human CD4 transgenic mice induced by HIV-gp120 and gp120-specific antibodies from AIDS patients

AUTHOR(S): Wang, Zhi-qin; Orlikowsky, Thorsten; Dudhane, Anita; Mittler, Robert; Blum, Michelle; Lacy, Elizabeth; Riethmueller, Gert; Hoffmann, Michael K.

CORPORATE SOURCE: Dep. Microbiology Immunology, New York Med. Coll., Valhalla, NY, 10595, USA

SOURCE: European Journal of Immunology (1994), 24(7), 1553-7
CODEN: EJIMAF; ISSN: 0014-2980

DOCUMENT TYPE: Journal

LANGUAGE: English

AB CD4, a T cell receptor for major histocompatibility complex class II antigen, is a key regulator of immunol. reactivities. When engaged together with the T cell antigen receptor, CD4 enhances immune reactions, whereas when ligated independently of the antigen receptor CD4 inhibits the activation of T cells or initiates their deletion. CD4 serves also as a receptor for the human immunodeficiency virus (HIV), which binds the receptor with high avidity through its envelope mol., gp120. Studies in tissue culture have

shown that its affinity to CD4 gives the virus opportunities to utilize CD4-mediated signaling and to manipulate immunocytes. The authors show here in human CD4 transgenic mice that appropriately cross-linked HIV envelope protein causes massive deletion of HIV-reactive T cells in vivo.

L4 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1992:253660 CAPLUS

DOCUMENT NUMBER: 116:253660

TITLE: Synthetic peptides of human CD4 enhance binding of Ig to monocyte/macrophage cells. I. Characterization and mapping studies

AUTHOR(S): Lenert, Petar; Mehta, Ravindra L.; Zanetti, Maurizio

CORPORATE SOURCE: Dep. Med., Univ. California, San Diego, CA, 92103, USA

SOURCE: Journal of Immunology (1992), 148(6), 1759-63

CODEN: JOIMA3; ISSN: 0022-1767

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Human T cell glycoprotein CD4 binds to class II MHC mols. and to HIV envelope protein gp120. CD4 and synthetic peptides corresponding to amino acid residues 21-49 of the first extracellular domain of CD4, also bind Ig and, with greater avidity, antibody:Ag complex. The authors investigated the effect of CD4 synthetic peptides on the binding and uptake of human Ig by monocyte/macrophage U937 cells. A synthetic peptide corresponding to amino acid residues 21-49 enhanced binding to U937 cells of both aggregated and nonaggregated Ig. The enhancement was concentration dependent, occurred both in normal and low ionic strength conditions, and varied with the time and the temperature of the preincubation step. The enhancement was maximal after preincubation for 3 h at 37°. A peptide concentration of 20 µg/mL was sufficient for optimal binding of both nonaggregated and aggregated Ig. CD4 peptide 21-49 also enhanced binding of Ig to Staphylococcus aureus protein A. These studies open a new perspective in the way monocyte/macrophage cells handle Ig, antibody:Ag, or Id:anti-Id complex, in particular when present at threshold amts. in a nonpptg. form.

L4 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1990:476178 CAPLUS

DOCUMENT NUMBER: 113:76178

TITLE: Human CD4 binds immunoglobulins

AUTHOR(S): Lenert, Petar; Kroon, Daniel; Spiegelberg, Hans;

Golub, Edward S.; Zanetti, Maurizio

CORPORATE SOURCE: Dep. Med., Univ. California, San Diego, CA, 92103, USA

SOURCE: Science (Washington, DC, United States) (1990),

248(4963), 1639-43

CODEN: SCIEAS; ISSN: 0036-8075

DOCUMENT TYPE: Journal

LANGUAGE: English

AB T cell glycoprotein CD4 binds to class II major histocompatibility mols. and to the human immunodeficiency virus (HIV) envelope protein gp120. Recombinant CD4 (rCD4) bound to polyclonal immunoglobulin and 39 of 50 (78%) human myeloma proteins. This binding depended on the Fab and not the Fc portion of Ig and was independent of the light chain. Soluble rCD4, HIV gp120, and sulfated dextrans inhibited the CD4-Ig interaction. With the use of a panel of synthetic peptides, the region critical for binding to Ig was localized to amino acids 21 to 38 of the first extracellular domain of CD4. CD4-bound antibody (Ab) complexed with antigen approx. 100 times better than Ab alone. This activity may contribute to the Ab-mediated enhancement of cellular HIV interaction that appears to depend on a trimol. complex of HIV, antibodies to gp120, and CD4.

=> FIL STNGUIDE
COST IN U.S. DOLLARS

| SINCE FILE | TOTAL |
|------------|---------|
| ENTRY | SESSION |
| 83.04 | 83.25 |

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

| SINCE FILE | TOTAL |
|------------|---------|
| ENTRY | SESSION |
| -17.16 | -17.16 |

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